Appl. No.	:	09/747,383	Confirmation No. 9470	
Applicant	:	Vlasselaer et al.		
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Examiner	:	SEHARASEYON, J.		
Docket No.	:	13903.0034USU1		
Customer No.	:	23552		

CERTIFICATE UNDER 37 CFR 1.8:
I hereby certify that this correspondence is being transmitted via facsimile to the Commissioner for Patents, TC__ on 2/24/04.
By: James Larkin

DECLARATION OF PETER VAN VLASSELAER UNDER 37 C.F.R. § 1.132

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Peter Van Vlasselaer, of Sunnyvale, California, do declare and say as follows:

1. I am a research scientist employed by Intermune, Inc., and a co-inventor of the subject matter of U.S. Patent Application No. 09/747,383 filed December 22, 2000.

2. I understand that the Patent Examiner has rejected claims to compositions comprising gamma-IFN and characterized by an aerosol of aqueous droplets as obvious over *Huland* et al. (U.S. Patent No. 5,780,012) in view of both Debs et al. (J. of Imm. Vol. 140:3482-3488)) and Ruskewicz et al. (U.S. Patent No. 5,971,951). I have read and understood these publications.

3. The biologically active form of gamma-IFN is made up of two monomers that are held together by a non-covalent bond. At the time of the invention, it was known in the art

that shear forces and other physico-chemical challenges, such as those encountered during attempts to aerosolize a liquid gamma-IFN solution, are not well tolerated by the molecule. Upon aerosolization, these physico-chemical challenges can result in the conversion of gamma -IFN to its inactive monomeric form. Therefore, it is important to find ways to maintain the activity of a gamma-IFN solution upon aerosolization.

4. One way to increase the stability of gamma-IFN to aerosolization is through the addition of stabilizing agents such as high molecular weight molecules. Stabilizing agents can maintain the activity of gamma-IFN after aerosolization. Historically, human serum albumin (HSA) has been used in this manner. Since administration of HSA can cause infection in patients, safety concerns require an alternative to these solutions.

5. The present claims recite an aerosol composition formed from an aqueous gamma-IFN solution that contains, as a stabilizing agent, sugar, alcohol, amino acid, or a combination of these. The claimed composition has a gamma-IFN biological activity substantially the same as that of the original gamma -IFN solution. At the time of the invention, it was not publicly known or published that a gamma-IFN aerosol composition could be formulated using only sugar, alcohol, amino acid, or combination of these as a stabilizing agent, while maintaining a gamma-IFN biological activity substantially the same as that of the original gamma-IFN solution.

6. I understand that the Patent Examiner asserts that *Huland* et al. (U.S. Patent No. 5,780,012) teach aerosol compositions that may contain sugar, amino acids, and alcohol. According to my understanding, *Huland* et al. disclose the use of serum protein as the stabilizing agent. *Huland* et al. do not appear to teach the use of sugars, amino acids, alcohols, or a combination of these as stabilizing agents in place of serum proteins. *Huland* et al. do not appear to teach that sugars, amino acids, alcohols, or a combination of these are used as, or could be used as, stabilizing agents in the compositions.

7. I understand that the Patent Examiner asserts there is no teaching in *Huland* et al. to indicate that the biological activity of the cytokine in the aerosol composition is

substantially different from that of the solution. I understand *Huland* et al. to teach, however, that the serum protein can only be omitted when very high levels of cytokine (at least 0.5 mg/ml) are used and still allow recovery and biological activity of the drug (column 5, lines 37-39). Therefore, it is my understanding that this reference teaches that the omission of serum protein results in an aerosol composition having cytokine activity substantially less than that of the original cytokine solution.

8. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, under penalty of fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Date: 2/16/04

Peter Van Vlasselaer